

Serial No. 10/047,902

August 25, 2004

Amendment A

REMARKS

Claims 1-6, 8-48 and 60-64 are pending in the application. Applicants have amended claim 1 to overcome the rejection under 35 U.S.C. §102(b). The Examiner is respectfully requested to reconsider and withdraw the rejections in view of the amendments and remarks contained herein.

Amendments to Claims

Claims 1, 8 and 63 are amended and claim 7 is canceled in this response. Claim 1 is amended to incorporate the limitations of canceled claims 7. Claim 8 is amended to be dependent from claim 1 rather than canceled claim 7. Claim 63 is amended to provide proper antecedent basis. No new matter has been added. Upon entry of this amendment, claims 1-6, 8-48 and 60-64 will be pending in the application.

Information Disclosure Statement

Applicants acknowledge the Examiner's objection to the Information Disclosure Statement. A corrected Information Disclosure Statement is being submitted to the Office under separate cover.

Rejection under 35 U.S.C. §112, second paragraph

Claims 2-43 and 60-63 are rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. In particular, the claims are rejected because the Examiner is unclear as to whether the substituted cellulosic polymer is a component of the emulsion or of the capsule wall as recited in claims 22-24.

Applicants submit that the claims are definite. As stated at page 10, line 11 of the specification, "the cellulosic polymer can be suspended or dissolved in the liquid formulation of the invention, or alternatively, the substituted cellulosic polymer may be present as a component of the wall of the capsule wherein a liquid formulation of the invention is encapsulated." Thus, the cellulosic polymer may be present as a component of either the liquid formulation or the wall of the capsule or both. Reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph is respectfully requested.

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Serial No. 10/047,902

August 25, 2004

Amendment A

Claim 63 has been amended to obviate the antecedent basis objection and to indicate that the liquid fill composition is contained in the water-soluble capsule defined by claim 21.

Rejections under 35 U.S.C. §102(b)

1. Straub et al.

Claims 1-11, 21, and 64 stand rejected under 35 U.S.C. §102(b) as being anticipated by Straub et al. (U.S. Pat. No. 6,610,317). The rejection is respectfully traversed in view of the amendment to claim 1 and the reasons set forth below.

In order to be anticipating, a prior art reference must teach each and every element of the claimed invention. (MPEP §2131.01) In the instant application, amended claim 1 is directed to a pharmaceutical composition for administering paclitaxel comprising (a) paclitaxel or an analog thereof, (b) a pharmaceutically acceptable surfactant, (c) a pharmaceutically acceptable solvent, and (d) a substituted cellulosic polymer wherein the ratio of paclitaxel to surfactant is from about 1:3 to about 1:20. The composition of the present invention is novel over the cited reference, Straub (U.S. Patent No. 6,610,317), which describes pharmaceutical compositions comprising a porous matrix form of paclitaxel without the solubilizing agent, CREMOPHOR™. In particular, Straub does not describe compositions of paclitaxel having a weight ratio of paclitaxel to surfactant of about 1:3 to about 1:20. Thus, it is respectfully submitted that the cited reference does not teach every element of claim 1 such that claims 1-11, 21 and 64 are not anticipated. Reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) is requested.

2. Lambert et al.

Claims 1-11, 21, and 64 are further rejected under 35 U.S.C. §102(b) as anticipated by Lambert et al. (U.S. Patent No. 6,660,286). The rejection is respectfully traversed in view of the amendment to claim 1 and the reasons set forth below.

The cited reference, Lambert, describes pharmaceutical compositions comprising a tocopherol (Vitamin E), a surfactant or mixtures of surfactants incorporating a co-solvent and a therapeutic agent. As stated by the Examiner, Lambert is missing the express teaching of a substituted cellulosic polymer in combination with the above ingredients. Thus, Lambert et al.

Serial No. 10/047,902
August 25, 2004
Amendment A

do not teach each and every element of the instantly defined claims such that the present invention is not anticipated. Reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) is requested.

Rejections under 35 U.S.C. §103(a)

1. Lambert et al.

Claims 1-11, 21, and 64 stand rejected under 35 U.S.C. §103(a) as obvious over Lambert et al. (U.S. Patent No. 6,660,286). The rejection is respectfully traversed for the reasons set forth below.

As defined in claim 1, the present invention is directed to a pharmaceutical composition for administering paclitaxel comprising (a) paclitaxel or an analog thereof, (b) a pharmaceutically acceptable surfactant, (c) a pharmaceutically acceptable solvent, and (d) a substituted cellulosic polymer wherein the ratio of paclitaxel to surfactant is from about 1:3 to about 1:20. In particular, Applicants have found that the presence of a substituted cellulosic polymer, which is used as a crystallization inhibitor, advantageously and substantially improves the bioavailability of paclitaxel and permits a reduction in the amount of the surfactant which is known to cause undesirable side effects when administered orally in large amounts. See, specification at page 11, line 24 to page 12, line 4.

In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the teachings of prior art references; and the references, when combined, must teach all of the claim limitations. See MPEP 2143. Applicants submit that the instant claims are not obvious in view of Lambert. Nothing in the reference teaches or suggests the compositions of the present invention comprising (a) paclitaxel or an analog thereof, (b) a pharmaceutically acceptable surfactant, (c) a pharmaceutically acceptable solvent, and (d) a substituted cellulosic polymer wherein the ratio of paclitaxel to surfactant is from about 1:3 to about 1:20. Thus, as further described below, Applicants submit the cited reference does not contain the necessary suggestion or motivation to practice the present invention.

Serial No. 10/047,902
August 25, 2004
Amendment A

The Examiner contends that it would have been obvious to have used both a solvent, such as PEG 400 and a substituted cellulosic polymer, such as Povidone, in the same composition because Lambert teaches that both substances modify the solubility behavior of paclitaxel and can thus be used as solvents for paclitaxel. However, nothing in the cited reference describes the use of a cellulosic polymer as a crystallization inhibitor. As stated above, Applicants have discovered that the use of a cellulosic polymer such as Povidone can act as a crystallization inhibitor, thereby reducing the amount of surfactant required in the composition. Thus, the cited reference does not provide any teaching with respect to the compositions of the present invention wherein a solvent and a cellulosic polymer are used independently.

Further, Lambert specifically teaches away from the compositions of the present invention. In particular, the compositions of the present invention describe the use of PEG-400 and ethanol as the solvent for paclitaxel. Lambert specifically teaches away from compositions containing monohydric alcohol. See, for example, column 11, line 61, wherein Lambert states that the compositions "are generally free of any monohydric alcohol." Accordingly, Lambert contains no motivation or suggestion to combine the disclosed ingredients in the appropriate amounts such that one skilled in the art would be motivated to make the claimed compositions of the present invention.

Because the cited reference does not provide the necessary suggestion or motivation to make the claimed compounds and the reference in fact teaches away from the claimed compositions, Applicants submit that claims 1-11, 21 and 64 are not obvious in view of Lambert et al., U.S. Patent No. 6,660,286. Reconsideration and withdrawal of the rejection is requested.

2. Lambert et al. in view of Kunz et al.

Claims 1-14, 18, 21-24, and 44-45 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Lambert et al in view of Kunz et al (U.S. Patent Application No. 2002/0025979). This rejection is respectfully traversed for the reasons set forth below.

Applicants submit that the deficiencies of the principal reference, Lambert et al., as described above cannot be overcome by resorting to the teachings of Kunz et al. Kunz describes a therapeutic method comprising administering a cytoskeletal inhibitor, such as taxol or a cytochalasin, to a procedurally traumatized, e.g. by an angioplasty procedure, mammalian vessel.

Serial No. 10/047,902

August 25, 2004

Amendment A

Nothing in the reference teaches or suggests a composition of the present invention as defined by claim 1. The Examiner is relying on Kunz to provide the necessary suggestion or motivation to use HPMC as a cellulosic polymer as defined in the present invention. However, HPMC is merely disclosed by Kunz et al. within a laundry list of acceptable inactive excipients or diluents for use in combination with a cytochalisin. See paragraph 0167 of the reference. Nothing in the reference remotely teaches or suggests the use of a cellulosic polymer for use in a paclitaxel composition as defined by the instant invention. Accordingly, one skilled in the art would not be motivated to combine the teachings of Kunz et al. with Lambert et al. to arrive at the present invention. Therefore, it is respectfully submitted that claims 1-14, 18, 21-24, and 44-45 are patentable over Lambert et al. in view of Kunz et al. Reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) is requested.

3. Lambert et al. in view of Kunz et al. and Broder et al.

Claims 1, 2, and 34-39 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Lambert et al in view of Kunz et al, and further in view of Broder et al (U.S. Patent No. 6,395,770). This rejection is respectfully traversed for the reasons set forth below.

Applicants submit that the deficiencies of the principal reference, Lambert et al., as described above cannot be overcome by resorting to the teachings of Kunz et al. and Broder et al. As stated above, nothing within Kunz remotely teaches or suggests the use of a cellulosic polymer for use in a paclitaxel composition as defined by the instant invention. Moreover, Broder describes a method to increase the systemic availability of orally administered taxanes, such as paclitaxel, by administering cyclosporin A either immediately after and/or before the drug. Nothing within the reference teaches or suggests a paclitaxel composition as defined by the instant invention. The Examiner is relying on Broder to provide the necessary suggestion or motivation to formulate an oral dose of paclitaxel at 10-700mg/gm. The present invention does not teach a range of 10-700mg/gm, but rather a range up to 100mg/gm of paclitaxel. Further, Broder teaches a range of 2-30mg/kg of patient body weight or body surface area. See column 9, line 48. This renders the dosage of paclitaxel indefinite as body weight or body surface area may vary. For example, a 130 lb(60 kg) person could receive between 120 to 1800mgs of paclitaxel under the teaching of the cited reference, which is well above the range disclosed by the present

Serial No. 10/047,902

August 25, 2004

Amendment A

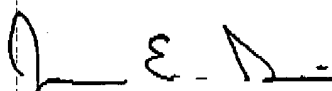
invention. Nothing in the reference remotely teaches the specific range of paclitaxel for use in a composition as defined by the instant claims. Accordingly, one skilled in the art would not be motivated by the teachings of Broder et al. and Kunz et al. with Lambert et al. to arrive at the present invention. Therefore, it is respectfully submitted that claims 1, 2, and 34-39 are patentable over Lambert et al. in view of Kunz et al. and Broder et al. Reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) is requested.

Conclusion

It is believed that all of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot by this Amendment. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all presently outstanding rejections. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (314) 446-7683.

The Commissioner is hereby authorized to charge \$980.00 for the purchase of a three-month extension of time under 37 C.F.R. 1.136(a) to Deposit Account No. 08-0750. Further, if Applicants owe any other fee(s), the Commissioner is hereby authorized to charge such fee(s) to Deposit Account No. 08-0750. In addition, if there is ever any other fee deficiency or overpayment of fees at any time during the prosecution of this patent application, the Commissioner is hereby authorized to charge any such fee deficiency or credit any such overpayment of fees to Deposit Account No. 08-0750.

Respectfully submitted,



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